

A Review: Medicinal Importance of *Glycyrrhiza glabra L.* (Fabaceae Family)

Muhammad Parvaiz, Khalid Hussain, Saba Khalid, Nigam Hussain,
Nukhba Iram, Zubair Hussain and Muhammad Azhar Ali

Department of Botany, Institute of Chemical and Biological Sciences (ICBS),
University of Gujrat (UOG), Gujrat 50700, Pakistan

Abstract: *Glycyrrhiza glabra L.* usually known as Mulaithi, Yashtimadu or licorice is a common herb, which has since long been used in traditional Ayurvedic and Chinese medicine for its mystic effects to cure numerous diseases such as hepatitis C, ulcers, pulmonary and skin diseases etc. The herb has been used in medicines for thousands of years. Its roots comprises of a compound that is 50 times sweeter than sugar. Significant constituents isolated from licorice include flavanoids, iso flavonoids, saponins, tripentenenes and the most imperative is Glycyrrhizin. Due to these elements it has important pharmacological activities such as antioxidant, antibacterial, antiviral and antiinflammatory as well.

Key words: *Glycyrrhiza glabra L.* Antibacterial • Antiviral Activities • Pakistan

INTRODUCTION

Glycyrrhiza glabra L. (Fabaceae) generally known as Mulaithi or Liquorice is a small perennial herb native to the Mediterranean region, central and southwest Asia. This herb is cultivated in Italy, Russia, France, UK, USA, Germany, Spain, China and Northern India. Large scale viable cultivation is seen in Spain, England and Sicily [1]. Mulaithi occupies the land for a period of five or sometimes four years. A yield of 2 tons of roots per acre for bailing, plus (3-4 centum) weight of trimmings or offal is considered adequate [2]. The conventional method for propagation of *Glycyrrhiza glabra L.* is via seed. Though, poor germination potential restricts its reproduction [3]. The rhizomes and roots of *Glycyrrhiza glabra L.* has been studied with respect to passive avoidance and spatial learning [4], anxiolytic activity [5], memory improvement [6], primary free radical foraging [7], cerebral ischemia [8] and antioxidant activity towards LDL oxidation [9]. The rhizomes and roots of this herb comprise of main active component glycyrrhizin, utilized commercially as a non-nutritional sweetener and flavoring agent in some candies and pharmaceuticals [10- 14]. Varied therapeutic properties of *G. glabra L.* for example antiallergy, anticarcinogenesis, antidiabetic, anti-inflammatory, antiulcer, laxative and antipyretic have attracted entrepreneurs to set eyes on this medicinal herb [15-17].

Mulaithi is a famous medicinal herb that grows in numerous parts of the world. It is one of the oldest and widely used herb from the earliest medical history of Ayurveda, both as a medicine and also as a flavoring to disguise the unpleasant flavor of other medications [18]. Yashtimadu has been shown to have great antioxidant, free radical scavenging [19, 20], and anticonvulsant activities [21, 22]. It has been shown to minimize circulating levels of testosterone in men [23-25].

Anti-oxidant and Anti-bacterial Activity: Hydromethanolic root extract of *Glycyrrhiza glabra L.* showed existence of numerous useful secondary metabolites such as: flavonoids, saponins, alkaloids and so on. Because of these constituents the extract exhibited effective anti-oxidant and anti-bacterial activities. It is able to fight against scavenging hydroxyl radical and bacterial infection. It may be a significant remedy for inhibition of bacterial infection and scavenging of hydroxyl radicals which are produced during carcinogenesis [26].

Antiviral Activity: *Glycyrrhiza glabra L.* has a prominent antiviral activity as it does not allow the virus cell binding. It has been reported as (HIV-1) Japanese encephalitis virus and yellow fever virus. In past, antiviral activities of pyraziofurin, ribavirin, 6-azauridine, mycophenolic acid and glycyrrhizin against 2 clinical isolates of 'SARS'

(Severe Acute Respiratory Syndrome) virus (FFM-1 & FFM-2) from patients with Severe Acute Respiratory Syndrome admitted to clinical center of Frankfurt University, Germany were assessed and it was observed that glycyrrhizin was the most effective in controlling viral replication and could be used as a prophylactic measure, glycyrrhizin has been formerly used to treat patients suffering from (HIV-1 & chronic hepatitis C) virus [27- 29]. Yashtimadu has been reported to have a direct hepatoprotective effect [30].

Antiinflammatory Activity: β -glycyrrhritinic acid has displayed antiinflammatory properties in different animal models [31- 33]. β -Glycyrrhritinic acid is the major metabolite of glycyrrhizin [34]. Two mechanisms have been recommended for the antiinflammatory effects of β -glycyrrhritinic acid, First, it inhibits glucocorticoid metabolism and potentiates their effects. This potentiation was reported in skin and lung after co-administration of them with β -glycyrrhritinic acid [35, 39]. Since, β -glycyrrhritinic acid is a potent inhibitor of 11β - hydroxysteroid hydroxylase [36], it causes an accumulation of glucocorticoids with antiinflammatory properties. Oral administration of β -glycyrrhritinic acid or glycyrrhizin confirmed this result [37]. Second, it inhibits classical complement pathway activation and its activity is dependent on its conformation [38]. Thus, it is suggested that co medication of it with hydrocortisone in the treatment of inflammatory lung disease will be useful [39]. Glycyrrhizin inhibited reactive oxygen species (ROS) generation by neutrophils which are the potent mediator of tissue inflammation in the *in vitro* study. It was thought that one of its antiinflammatory effect was due to this inhibitory effect [15,40]. Also, the generation of (ROS) was also suppressed by glabridin treatment in (RAW 264.7) cells [41]. *Glycyrrhiza glabra L.* and glyderinine, a derivative of glycyrrhizic acid, showed an antiinflammatory effect [42, 43]. It also reduced myocardial inflammatory edema in experimental myocardial damage [44]. In addition, glabridin and licochalcone A have shown an anti-inflammatory effect in *in vivo* studies [45, 41].

Pharmacological Activities: Chronic Hepatitis in Japan, glycyrrhizin has been used for more than 60 years as a treatment for chronic hepatitis C [64-65]. Stronger Neo-Minophagen C (SNMC), a glycyrrhizin preparation, has been extensively used with considerable success. In two clinical trials, SNMC has been shown to significantly lower aspartate transaminase (AST), alanine

transaminase (ALT) and gammaglutamyltransferase (GGT) concentrations, while simultaneously ameliorating histologic evidence of necrosis and inflammatory lesions in the liver [46, 47]. In recent years, several studies have been performed supporting this action [47]. Previously, interferon (IFN) therapy is a predominant treatment for chronic hepatitis. Because its efficacy is limited, an alternative treatment is desirable. SNMC has profound effects on the suppression of liver inflammation and is effective in improving chronic hepatitis and liver cirrhosis. It also appears to have considerably fewer side effects than IFN [48].

Antidemulcent Andantitussive Activity: The extract of the crushed drug in water was found to be effective in the treatment of sore throat cough bronchial catarr. It is antitussive and expectorant loosening tracheal mucus secretion. The demulcent action is attributed to glycyrrhizin [47].

Active Components

Flavonoids: Other components include flavonoids and chalcones (Which are responsible for the yellow color of licorice) such as liquiritin, rhamnoliquiritin, neoliquiritin, liquiritigenin, chalcones isoliquiritin, isoliquiritigenin, neoisoliquiritin, licuraside, glabrolide and licoflavonol [49]. Previously, 5,8-dihydroxy-flavone-7-O-beta-D-glucuronide, glychionide A and 5-hydroxy-8- methoxyl-flavone-7-O-beta-D-glucuronide, glychionide B were isolated from the roots of *G. glabra*. The retrochalcones, licochalcone A, B, C, D and echinatin, were recently isolated from the roots of *G. inflata* [50, 51] and the minor flavonoids, isotrifoliol and glisoflavanone, from the underground part of *G. uralensis* [52].

Isoflavones: Isoflavonoid derivatives present in licorice include glabridin, galbrene, glabrone, shinpterocarpin, licoisoflavones A and B, formononetin, glyzarin, kumatakenin [49]. Some years ago, hispaglabridin A, hispaglabridin B, 4'-O-methylglabridin and 3'- hydroxy-4'-O-methylglabridin [51, 53] and glabroiso flavanone A and B glabroiso-flavanone B [54], have been found.

Saponins: Licorice root contains triterpenoid saponins (4-20%), mostly glycyrrhizin, a mixture of potassium and calcium salts of glycyrrhizic acid (also known as glycyrrhizic or glycyrrhizinic acid and a glycoside of glycyrrhretinic acid) which is 50 times as sweet as sugar [55]. Other triterpenes present are liquiritic acid, glycyrrretol, glabrolide, isoglabrolide and licorice acid [49].

Recently, it was shown that high concentration glycyrrhizin production is possible within a very short production period under controlled environments [56].

Traditional Uses: Traditionally the plant has been recommended as a prophylaxis for gastric and duodenal ulcers and dyspepsia as an anti-inflammatory agent during allergic reactions [57]. In folk medicine, it is used as a laxative, emmenagogue, contraceptive, galactagogue, anti-asthmatic drug and antiviral agent [58]. The medicinal plants are being used in many diseases from hundred years before [66]. Glycyrrhiza roots are used for its demulcent and expectorant property [59]. It is useful in anemia, gout, sore throat, tonsillitis, flatulence, sexual debility, hyperdyspsia, fever, coughs, skin diseases, swellings, acidity, leucorrhoea, bleeding, jaundice, hiccough, hoarseness, bronchitis, vitiated conditions of vata dosha, gastralgia etc [60]. It is an important ingredient in medicinal oils for the epilepsy, paralysis, rheumatism, hemorrhagic diseases and also used in the treatment of diarrhea, fever with delirium and anuria available from [59]. Research shows that on being broken down in the gut, glycyrrhizin exerts an anti-inflammatory action similar to hydrocortisone and other corticosteroid hormones. It stimulates production of hormones by adrenal glands and reduces the breakdown of steroids by the liver and kidneys. Glycyrrhizin also proved effective in the treatment of chronic hepatitis and liver cirrhosis [61]. For relieving pain, discomfort and other symptoms caused by acrid matter in the stomach, Glycyrrhiza glabra is considered as one of the best remedies. It seems to remove the irritating effects of acids in a better way than alkalies [62]. It is used by practitioners of the indigenous systems as tonic, as a demulcent in catarrh of the genitor-urinary passages and as a mild laxative [63].

CONCLUSION

Glycyrrhiza glabra L. is extensively used and a potent therapeutic herb used in many ailments of different systems. It is used as a single remedy and also as a chief content in many medicinal preparations like lozenges, syrups etc. It is in great demand internationally as remedial and nutritious supplement. This herb has been used since centuries for bronchitis, ulcers, asthma and an anti-inflammatory. It is reported to contain essential coumarins, oil, alkaloids and flavonoids. Extract of root can be found in different herbal preparations that are in market today. The clinical and pharmacologic studies

described in the present review confirm the medicinal value of *Glycyrrhiza glabra L.* It is a significant source of different types of compounds with varied chemical structures as well as pharmacologic properties. Existence of such a wide range of chemical compounds shows that the plant could serve as a lead for the development of novel agents having good efficacy in different disorders in the coming years.

REFERENCES

1. Chopra, R.N. and I.C. Chopra, 1958. Indigenous drugs of India. Second edition. Kolkata: Academic Publishers, pp: 183-187.
2. Vispute, S. and A. Khopade, 2011. Glycyrrhiza glabra Linn. - "Klitaka": a review. Int J Pharma Bio Sci., 2: 42-50.
3. Sawaengsak, W., T. Saisavoey, P. Chuntarat and A. Karnchanatat, 2011. Micropropagation of the medicinal herb Glycyrrhiza glabra L. through shoot tip explant culture and glycyrrhizin detection. Int. Res. J. Plant Sci., 2: 129-136.
4. Ravichandra, V. Ahalyadevi and S. Adiga, 2007. Evaluation of the effect of Glycyrrhiza glabra Linn root extract on spatial learning and passive avoidance response in rats. Indian Drugs, 44: 214-19.
5. Ambawade, K.D. Kasture and V.S. Kasturi, 2001. Anxiolytic activity of Glycyrrhiza glabra Linn. J Nat Remedies, 2: 130-34.
6. Dinesh, D., P. Milind and S.K. Kulkarni, 2004. Memory enhancing activity of Glycyrrhiza glabra in mice. J Ethnopharmacol, 91: 361 -65.
7. Toshio, F., S. Kazue and N. Taro, 2003. Preliminary evaluation of anti nephritis and radical scavenging activities of glabridin from Glycyrrhiza glabra Linn. Fitoterapia, 74: 624-29.
8. Zhan, C. and J. Yang, 2006. Protective effects of isoliquiritigenin in transient middle cerebral artery occlusion induced focal cerebral ischemia in rats. Pharmacol. Res., 53: 303-09. <http://dx.doi.org/10.1016/j.phrs.2005.12.008>.
9. Vaya, J., P.A. Belinky and M. Aviram, 1998. Structural aspects of the inhibitory effect of glabridin on LDL oxidation. Free Rad. Biol. Med., 24: 1419-29.
10. Wang, Z.Y., M. Athar and D.R. Bickers, 2000. Licorice in foods and herbal drugs: Chemistry, pharmacology, toxicology and uses. In Herbs, Botanicals & Teas, Mezza G, Oomah BD (eds). Technomic Publishing Co. Inc: Lancaster, pp: 321-353.

11. Winston and David, 2007. Steven Maimes. Adaptogens. Herbs for strength, stamina and stress relief. Healing Arts Press. ISBN 978-1-59477-158-3.
12. Krausse, R., J. Bielenberg, W. Blaschek and U. Ullmann, 2004. In vitro anti-Helicobacter pylori activity of extractum liquiritiae, glycyrrhizin and its metabolites. The Journal of Antimicrobial Chemotherapy, 54(1): 243- 264.
13. Wang, G.S. and Z.W. Han, 1993. The protective action of glycyrrhiza flavonoids against carbon tetrachloride hepatotoxicity in mice. Yao. Xue. Xue. Bao, 28: 572-576.
14. Asl, M.N. and H. Hosseinzadeh, 2008. Review of pharmacological effects of Glycyrrhiza sp. and its bioactive compounds. Phytotherapy Research, 22: 709-724.
15. Wang, Z.Y. and D.W. Nixon, 2001. Licorice and cancer. Nutr Cancer, 39: 1-11.
16. Brown, D., 1995. The herb national society of America encyclopedia of herbs and their uses. Dorling Kindersley Publishing Inc. New York, pp: 135.
17. Chopra, R.N., S.L. Nayar and I.C. Chopra, 2002. Glossary of Indian medicinal plants. NISCIR, CSIR.
18. Biondi, D.M., C. Rocco and G. Ruberto, 2005. Dihydrostilbene derivatives from Glycyrrhiza glabra leaves. Journal of Natural Products, 68: 1099-1102.
19. Haraguchi, H., H. Ishikawa, K. Mizutani, Y. Tamura and T. Kinoshita, 1998. Antioxidative and superoxide scavenging activities of retrochalcones in Glycyrrhiza inflata. Bioorganic& Medicinal Chemistry, 6: 339-347.
20. Di, M.M.V. and M.J. Fonseca, 2005. Assays of physical stability and antioxidant activity of a topical formulation added with different plant extract. Journal of Pharmaceutical and Biomedical Analysis, 37: 287- 295.
21. Nassiri-Asl, M., S. Saroukhani and F. Zamansoltani, 2007. Anticonvulsant effects of aqueous extract of Glycyrrhiza glabra root in PTZ-induced seizure in mice. International Journal of Pharmacology, 3: 432-434.
22. Das, S.K. V. Das, A.K. Gulati and V.P. Singh, 1998. Deglycyrrhizinated licuorice in aphthous ulcers. The journal of the associate ion of physicians of India, 37(10): 647.
23. Rafi, M.M., B.C. Vastano, N. Zhu, C.T. Ho, G. Ghai, R.T. Rosen, M.A. Gallo and R.S. DiPaola, 2002. Novel polyphenol molecule isolated from licorice root (Glycyrrhiza glabra) induces apoptosis, G2/M cell cycle arrest and Bcl-2 phosphorylation in tumor cell lines, J. Agric. Food Chem., 50: 677-684.
24. Armanini, D., G. Bonanni and M. Palermo, 1999. Reduction of serum testosterone in men by licorice, N. Engl. J. Med., 341: 1158.
25. Armanini, D., C. Fiore, M.J. Mattarello, J. Bielenberg and M. Palermo, 2002. History of the endocrine effects of licorice, Exp. Clin. Endocrinol. Diabetes 110: 257-261.
26. Sharma, V., R.C. Agrawal and S. Pandey, 2013. Phytochemical screening and determination of antibacterial and anti-oxidant potential of Glycyrrhiza glabra root extracts. J. Environ. Res. Develop, 7(4A): 1552-1558.
27. Clercq, E.D., 2000. Current lead natural products for the chemotherapy of human immunodeficiency virus (HIV) infection. Med. Res. Rev., 20: 323-349.
28. Badam, L., 1997. In vitro antiviral activity of indigenous glycyrrhizin, licorice and Glycyrrhizic acid (Sigma) on Japanese Encephalitis Virus. J. Commun. Dis., 29: 91-99.
29. Badam, L., 1994. In vitro studies on the effect of glycyrrhizin from Glycyrrhiza glabra on some RNA and DNA viruses. Indian J. Pharmacol., 26: 194-199.
30. Luper, S., 1999. A review of plants used in the treatment of liver disease: Part Two. Altern Med. Rev., 4: 178-188.
31. Capasso, F., N. Mascolo, G. Autore and M.R. Duraccio, 1983. Glycyrrhetic acid, leucocytes and prostaglandins. J. Pharm Pharmacol., 35: 332-335.
32. Amagaya, S., E. Sugishita, Y. Ogihara, S. Ogawa, K. Okada and T. Aizawa, 1984. Comparative studies of the stereoisomers of glycyrrhetic acid on anti-inflammatory activities. J/ Pharmacobiodyn, 79: 923-928.
33. Inoue, H., T. Mori, S. Shibata and Y. Koshihara, 1989. Modulation by glycyrrhetic acid derivatives of TPA-induced mouse ear oedema. Br J. Pharmacol, 96: 204-210.
34. Gumprich, E., R. Dahl, M.W. Devereaux and R.J Sokol, 2005. Licorice compounds glycyrrhizin and 18 β -glycyrrhetic acid are potent modulators of bile acid-induced cytotoxicity in rat hepatocytes. J. Biol. Chem., 280: 10556-10563.
35. Teelucksingh, S., A.D. Mackie, D. Burt, M.A. McIntyre, L. Brett and C.R. Edwards, 1990. Potentiation of hydrocortisone activity in skin by glycyrrhetic acid. Lancet, 335: 1060-1063.
36. Walker, B.R. and C.R. Edwards, 1991. 11 beta-Hydroxysteroid dehydrogenase and enzyme-mediated receptor protection: life after liquorice? Clin Endocrinol., 35: 281-289.

37. MacKenzie, M.A., W.H. Hoefnagels and P.W. Kloppenborg, 1990. Glycyrrhetic acid and potentiation of hydrocortisone activity in skin. *Lancet*, 335: 1534.
38. Kroes, B.H., C.J. Beukelman, A.J.J. Van Den Berg, G.J. Wolbink and R.P. Van Dijk Labadie, 1997. Inhibition of human complement by beta-glycyrrhetic acid. *Immunology*, 90: 115-120.
39. Schleimer, R.P., 1991. Potential regulation of inflammation in the lung by local metabolism of hydrocortisone. *Am J. Respir Cell. Mol. Biol.*, 4: 166-173.
40. Akamatsu, H., J. Komura, Y. Asada and Y. Niwa, 1991. Mechanism of anti-inflammatory action of glycyrrhizin: effects on neutrophil functions including reactive oxygen species generation. *Planta Med.*, 57: 119-121.
41. Jong, S.K., D.Y. Yeo and J.C. Ig, 2005. Glabridin, an isoflavan from licorice root, inhibits inducible nitric-oxide synthase expression and improves survival of mice in experimental model of septic shock. *J. Pharmacol. Exp. Ther.*, 312: 1187-1194.
42. Azimov, M.M., U.B. Zakirov and S.H.D. Radzhapova, 1988. Pharmacological study of the anti-inflammatory agent glycyrrhizine. *Farmakol Toksikol*, 51: 90-93.
43. Tokiwa, T., K. Harada, T. Matsumura and T. Tukiya, 2004. Oriental medicinal herb, *Periploca sepium*, extract inhibits growth and IL-6 production of human synovial fibroblast-like cells. *Pharm Bull*, 27: 1691-1693.
44. Zakirov, N.U., M.I. Aizimov and A.G. Kurmukov, 1999. The cardioprotective action of 18-dehydroglycyrrhetic acid in experimental myocardial damage. *Eksp Klin Farmakol*, 62: 19-21.
45. Furuhashi, I., S. Iwata, S. Shibata, T. Sato and H. Inoue, 2005. Inhibition by licochalcone A, a novel flavonoid isolated from licorice root, of IL-1 β -induced PGE₂ production in human skin fibroblasts. *J. Pharm Pharmacol.*, 57: 1661-1666.
46. Steve, H.N.D., 2005. Celiac disease and gluten associated diseases. *Alternative Medicine Review*, 10: 3.
47. Van Rossum, T.G., A.G. Vulto, W.C. Hop and S.W. Schalm, 2001. Glycyrrhizin-induced reduction of ALT in European patients with chronic hepatitis C. *Am J. Gastroenterol.*, 96: 2432-2437.
48. Iino, S., T. Tango and T. Matsushima, 2001. Therapeutic effects of stronger neo-minophagen C at different doses on chronic hepatitis and liver cirrhosis. *Hepatol. Res.*, 19: 31-40.
49. Williamson, E.M., 2003. Licorice. In *Potter's Cyclopedia of Herbal Medicines*. C W Daniels: Saffron Walden, UK, pp: 269- 271.
50. Li, J.R., Y.Q. Wang and Z.Z. Deng, 2005. Two new compounds from *Glycyrrhiza glabra*. *J. Asian Nat. Prod. Res.*, 7: 677-680.
51. Haraguchi, H., 2001. Antioxidative plant constituents. In *Bioactive Compounds from Natural Sources: Isolation, Characterization and Biological Properties*, Tringali C (ed.). Taylor and Francis: New York, pp: 348-352.
52. Hatano, T., Y. Aga, Y. Shintani, H. Ito, T. Okuda and T. Yoshida, 2000. Minor flavonoids from licorice. *Phytochemistry*, 55: 959-963.
53. De Simone, F., R. Aquino, N.D. Tommasi, N. Mahmood, S. Piacente and C. Pizza, 2001. Anti-HIV aromatic compounds from higher plants. In *Bioactive Compounds from Natural Sources: Isolation, Characterization and Biological Properties*, Tringali C (ED.). Taylor and Francis: New York, pp: 325.
54. Kinoshita, T., Y. Tamura and K. Mizutani, 2005. The isolation and structure elucidation of minor isoflavonoids from licorice of *Glycyrrhiza glabra* origin. *Chem. Pharm. Bull*, 53: 847- 849.
55. Blumenthal, M., A. Goldberg and J. Brinckmann, 2000. *Herbal Medicine: Expanded Commission E Monographs*. American Botanical Council: Newton, pp: 233-236.
56. Afreen, F., S.M.A. Zobayed and T. Kozai, 2005. Spectral quality and UV-B stress stimulate glycyrrhizin concentration of *Glycyrrhiza uralensis* in hydroponic and pot system. *Plant Physiol. Biochem*, 43: 1074-1081.
57. Ammosov, S. and V.I. Litvinenko, 2003. Triterpenoids of Plants of *Glycyrrhiza glabra* L. and *Meristotropis Fisch. Et Mey* Genuses. *Pharm Chem. J.*, 37: 83-94.
58. Saxena, S., 2005. *Glycyrrhiza glabra*: Medicine over the millennium. *Product Red*, 4: 358-367.
59. Sheetal, V. and K. Ashlesha, 2011. *Glycyrrhiza glabra* Linn- "KLITAKA": A review. *Inter Journal of Pharma and Bio Sciences*, 2(3): 42-51.
60. Sheth, A., 2005. *The Herbs of India*. 1st Edition, Vol.2. Gujrat: Hi Scan Pvt. Ltd. pp: 566.
61. Khare, C.P., 2004. *Encyclopedia of Indian Medicinal Plants*. New York: Springer-Verlag, pp: 233-5.
62. Chopra, R.N. and I.C. Chopra, 1958. *Indigenous Drugs of India*. Second ed. Kolkata: Academic Publishers, pp: 183-7.

63. Nadkarni, K.M., 1976. *Indian Materia Medica* Mumbai: Popular Prakashan Pvt. Ltd, pp: 582-4.
64. Van Rossum, T.G., A.G. Vulto, W.C. Hop, S.W. Schalm, 2001. Glycyrrhizin-induced reduction of ALT in European patients with chronic hepatitis C. *Am J. Gastroenterol.*, 96: 2432-2437.
65. Tsubota, A., H. Kumada, Y. Arase, *et al.*, 1999. Combined ursodeoxycholic acid and glycyrrhizin therapy for chronic hepatitis C virus infection: a randomized controlled trial in 170 patients. *Eur J Gastroenterol Hepatol.*, 11: 1077-1083.
66. Parvaiz, M., K. Hussain, M. Tufail, G. William, M. Shoaib and M.D. Jamil, 2013. Ethnobotanical Survey of Wild Plants Used to Cure Piles in District Gujrat, Punjab, Pakistan. *Global Journal of Pharmacology*, 7(3): 337-341.